




[PubMed](#)
[Nucleotide](#)
[Protein](#)
[Genome](#)
[Structure](#)
[PMC](#)
[Taxonomy](#)
[OMIM](#)
[Books](#)

Search for

Display Show

Range: from to Features: ☐ SNP ☒ CDD ☒ HPRD

☐ 1: [NP_066124](#). Reports ret proto-oncogen...[gi:10862703]

[BLink](#), [Conserved Domains](#), [Links](#)

[Comment](#) [Features](#) [Sequence](#)

LOCUS NP_066124 1114 aa linear PRI 15-FEB-2009
 DEFINITION ret proto-oncogene isoform a [Homo sapiens].
 ACCESSION NP_066124
 VERSION NP_066124.1 GI:10862703
 DBSOURCE REFSEQ: accession [NM_020975.4](#)
 KEYWORDS .
 SOURCE Homo sapiens (human)
 ORGANISM [Homo sapiens](#)
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
 Catarrhini; Hominidae; Homo.

REFERENCE 1 (residues 1 to 1114)
 AUTHORS Pigny,P., Cardot-Bauters,C., Do Cao,C., Vantyghem,M.C.,
 Carnaille,B., Pattou,F., Caron,P., Wemeau,J.L. and Porchet,N.
 TITLE Should genetic testing be performed in each patient with sporadic
 pheochromocytoma at presentation?
 JOURNAL Eur. J. Endocrinol. 160 (2), 227-231 (2009)
 PUBMED [19029228](#)
 REMARK GeneRIF: Observational study of gene-disease association. (HuGE
 Navigator)

REFERENCE 2 (residues 1 to 1114)
 AUTHORS Henderson,Y.C., Shellenberger,T.D., Williams,M.D., El-Naggar,A.K.,
 Fredrick,M.J., Cieply,K.M. and Clayman,G.L.
 TITLE High rate of BRAF and RET/PTC dual mutations associated with
 recurrent papillary thyroid carcinoma
 JOURNAL Clin. Cancer Res. 15 (2), 485-491 (2009)
 PUBMED [19147753](#)
 REMARK GeneRIF: Observational study of gene-disease association. (HuGE
 Navigator)

REFERENCE 3 (residues 1 to 1114)
 AUTHORS Ito,Y., Miyauchi,A., Yabuta,T., Fukushima,M., Inoue,H., Tomoda,C.,
 Urano,T., Kihara,M., Higashiyama,T., Takamura,Y., Miya,A.,
 Kobayashi,K. and Matsuzuka,F.
 TITLE Alternative surgical strategies and favorable outcomes in patients
 with medullary thyroid carcinoma in Japan: experience of a single
 institution
 JOURNAL World J Surg 33 (1), 58-66 (2009)
 PUBMED [19005720](#)
 REMARK GeneRIF: Observational study of gene-disease association. (HuGE
 Navigator)

REFERENCE 4 (residues 1 to 1114)
 AUTHORS Cincinelli,R., Cassinelli,G., Dallavalle,S., Lanzi,C., Merlini,L.,
 Botta,M., Tuccinardi,T., Martinelli,A., Penco,S. and Zunino,F.
 TITLE Synthesis, modeling, and RET protein kinase inhibitory activity of

3- and 4-substituted beta-carbolin-1-ones
JOURNAL J. Med. Chem. 51 (24), 7777-7787 (2008)
PUBMED [19053769](#)
REMARK GeneRIF: analysis of how RET protein kinase is inhibited by
beta-carbolin-1-ones
REFERENCE 5 (residues 1 to 1114)
AUTHORS Umansky,V., Abschuetz,O., Osen,W., Ramacher,M., Zhao,F., Kato,M.
and Schadendorf,D.
TITLE Melanoma-specific memory T cells are functionally active in Ret
transgenic mice without macroscopic tumors
JOURNAL Cancer Res. 68 (22), 9451-9458 (2008)
PUBMED [19010920](#)
REMARK GeneRIF: Melanoma-specific memory T cells are functionally active
in Ret transgenic mice without macroscopic tumors.
REFERENCE 6 (sites)
AUTHORS Kawamoto,Y., Takeda,K., Okuno,Y., Yamakawa,Y., Ito,Y., Taguchi,R.,
Kato,M., Suzuki,H., Takahashi,M. and Nakashima,I.
TITLE Identification of RET autophosphorylation sites by mass
spectrometry
JOURNAL J. Biol. Chem. 279 (14), 14213-14224 (2004)
PUBMED [14711813](#)
REFERENCE 7 (sites)
AUTHORS Iwashita,T., Kato,M., Murakami,H., Asai,N., Ishiguro,Y., Ito,S.,
Iwata,Y., Kawai,K., Asai,M., Kurokawa,K., Kajita,H. and
Takahashi,M.
TITLE Biological and biochemical properties of Ret with kinase domain
mutations identified in multiple endocrine neoplasia type 2B and
familial medullary thyroid carcinoma
JOURNAL Oncogene 18 (26), 3919-3922 (1999)
PUBMED [10445857](#)
REFERENCE 8 (sites)
AUTHORS Liu,X., Vega,Q.C., Decker,R.A., Pandey,A., Worby,C.A. and
Dixon,J.E.
TITLE Oncogenic RET receptors display different autophosphorylation sites
and substrate binding specificities
JOURNAL J. Biol. Chem. 271 (10), 5309-5312 (1996)
PUBMED [8621380](#)
REFERENCE 9 (residues 1 to 1114)
AUTHORS Itoh,F., Ishizaka,Y., Tahira,T., Yamamoto,M., Miya,A., Imai,K.,
Yachi,A., Takai,S., Sugimura,T. and Nagao,M.
TITLE Identification and analysis of the ret proto-oncogene promoter
region in neuroblastoma cell lines and medullary thyroid carcinomas
from MEN2A patients
JOURNAL Oncogene 7 (6), 1201-1206 (1992)
PUBMED [1350670](#)
REFERENCE 10 (residues 1 to 1114)
AUTHORS Santoro,M., Carlomagno,F., Hay,I.D., Herrmann,M.A., Grieco,M.,
Melillo,R., Pierotti,M.A., Bongarzone,I., Della Porta,G., Berger,N.
et al.
TITLE Ret oncogene activation in human thyroid neoplasms is restricted to
the papillary cancer subtype
JOURNAL J. Clin. Invest. 89 (5), 1517-1522 (1992)
PUBMED [1569189](#)
REFERENCE 11 (residues 1 to 1114)
AUTHORS Galland,F., Stefanova,M., Lafage,M. and Birnbaum,D.
TITLE Localization of the 5' end of the MCF2 oncogene to human chromosome
15q15----q23
JOURNAL Cytogenet. Cell Genet. 60 (2), 114-116 (1992)
PUBMED [1611909](#)
REFERENCE 12 (residues 1 to 1114)

AUTHORS Jhiang,S.M., Chiu,I.M. and Mazzaferri,E.L.
 TITLE An STS in the human PTC oncogene located at 10q11.2
 JOURNAL Nucleic Acids Res. 19 (15), 4303 (1991)
 PUBMED 1678508
 REFERENCE 13 (residues 1 to 1114)
 AUTHORS Tahira,T., Ishizaka,Y., Itoh,F., Sugimura,T. and Nagao,M.
 TITLE Characterization of ret proto-oncogene mRNAs encoding two isoforms
 of the protein product in a human neuroblastoma cell line
 JOURNAL Oncogene 5 (1), 97-102 (1990)
 PUBMED 2181380
 COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The
 reference sequence was derived from [DA100452.1](#), [BC003072.2](#),
[BC004257.1](#), [X12949.1](#), [AC010864.11](#) and [BM661773.1](#).

Summary: This gene, a member of the cadherin superfamily, encodes one of the receptor tyrosine kinases, which are cell-surface molecules that transduce signals for cell growth and differentiation. This gene plays a crucial role in neural crest development, and it can undergo oncogenic activation in vivo and in vitro by cytogenetic rearrangement. Mutations in this gene are associated with the disorders multiple endocrine neoplasia, type IIA, multiple endocrine neoplasia, type IIB, Hirschsprung disease, and medullary thyroid carcinoma. Two transcript variants encoding different isoforms have been found for this gene. Additional transcript variants have been described but their biological validity has not been confirmed. [provided by RefSeq].

Transcript Variant: This variant (2) represents the longer transcript and encodes the longer isoform (a). This isoform is also known as Ret51.

Publication Note: This RefSeq record includes a subset of the publications that are available for this gene. Please see the Entrez Gene record to access additional publications.

FEATURES Location/Qualifiers
 source 1..1114
 /organism="Homo sapiens"
 /db_xref="taxon:9606"
 /chromosome="10"
 /map="10q11.2"
 Protein 1..1114
 /product="ret proto-oncogene isoform a"
 /EC_number="2.7.10.1"
 /note="hydroxyaryl-protein kinase; RET transforming sequence; oncogene RET; cadherin family member 12; receptor tyrosine kinase; ret proto-oncogene (multiple endocrine neoplasia and medullary thyroid carcinoma 1, Hirschsprung disease)"
 /calculated_mol_wt=124188
 Region 43..264
 /region_name="CA"
 /note="Cadherin repeat domain; Cadherins are glycoproteins involved in Ca2+-mediated cell-cell adhesion; these domains occur as repeats in the extracellular regions which are thought to mediate cell-cell contact when bound to calcium; plays a role in cell...; cl02468"
 /db_xref="CDD:121330"
 Site order(43,102,104,129,151..152,245)
 /site_type="other"
 /note="Ca2+ binding site"

```

/db_xref="CDD:28913"
Region 173..358
/region_name="CA"
/note="Cadherin repeat domain; Cadherins are glycoproteins
involved in Ca2+-mediated cell-cell adhesion; these
domains occur as repeats in the extracellular regions
which are thought to mediate cell-cell contact when bound
to calcium; plays a role in cell...; cd00031"
/db_xref="CDD:28913"
Site order(178..179,230,232,264,266..267,300,302)
/site_type="other"
/note="Ca2+ binding site"
/db_xref="CDD:28913"
Site 687
/site_type="phosphorylation"
/experiment="experimental evidence, no additional details
recorded"
/citation=[8]
/db_xref="HPRD:01266"
Region 724..1005
/region_name="Pkinase_Tyr"
/note="Protein tyrosine kinase; pfam07714"
/db_xref="CDD:116328"
Region 728..1012
/region_name="PTKc_RET"
/note="PTKc_RET: Protein Tyrosine Kinase (PTK) family; RET
(rearranged during transfection) protein; catalytic (c)
domain. The PTKc family is part of a larger superfamily
that includes the catalytic domains of other kinases such
as protein serine/threonine...; cd05045"
/db_xref="CDD:88328"
Site order(730..734,738,756,758,804..805,807,811,874,878..879,
881,892,910..914,923,957)
/site_type="active"
/db_xref="CDD:88328"
Site order(730..733,738,756,758,804..805,807,811,881,892)
/site_type="other"
/note="ATP binding site"
/db_xref="CDD:88328"
Site 806
/site_type="phosphorylation"
/experiment="experimental evidence, no additional details
recorded"
/citation=[6]
/db_xref="HPRD:01266"
Site 809
/site_type="phosphorylation"
/experiment="experimental evidence, no additional details
recorded"
/citation=[6]
/db_xref="HPRD:01266"
Site 826
/site_type="phosphorylation"
/experiment="experimental evidence, no additional details
recorded"
/citation=[8]
/db_xref="HPRD:01266"
Site order(874,878,910..914,923,957)
/site_type="other"
/note="substrate binding site"

```

```

Site      /db_xref="CDD:88328"
          891..912
          /site_type="other"
          /note="activation loop (A-loop)"
          /db_xref="CDD:88328"
Site      900
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[6]
          /db_xref="HPRD:01266"
Site      905
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[6]
          /citation=[7]
          /citation=[8]
          /db_xref="HPRD:01266"
Site      981
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[6]
          /db_xref="HPRD:01266"
Site      1015
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[8]
          /db_xref="HPRD:01266"
Site      1029
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[8]
          /db_xref="HPRD:01266"
Site      1062
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[6]
          /citation=[8]
          /db_xref="HPRD:01266"
Site      1090
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[6]
          /db_xref="HPRD:01266"
Site      1096
          /site_type="phosphorylation"
          /experiment="experimental evidence, no additional details
          recorded"
          /citation=[6]
          /citation=[8]
          /db_xref="HPRD:01266"
CDS      1..1114
          /gene="RET"
          /gene_synonym="CDHF12; HSCR1; MEN2A; MEN2B; MTC1; PTC;

```

RET-ELE1; RET51"
/coded_by="NM_020975.4:191..3535"
/note="isoform a is encoded by transcript variant 2"
/db_xref="CCDS:CCDS7200.1"
/db_xref="GeneID:5979"
/db_xref="HGNC:9967"
/db_xref="HPRD:01266"
/db_xref="MIM:164761"

ORIGIN

```
1 makatsgaag lrlllllllp llgkvalgly fsrdaywekl yvdqaagtpl lyvhalrdap
61 eevpsfrlgq hlygtyrtrl hennwiciqe dtglllylnrs ldhsswekls vrnrgfpllt
121 vylkvflspt slregecqwp gcarvyfsff ntsfpacssl kprelcfpet rpsfirenr
181 ppgtfhqfrl lpvqflcpni svayrllege glpfrcapds levstrwald reqrekyelv
241 avctvhagar eevvmvpfpv tvydeddsap tfpagvdtas avvefkrked tvvatlrvfd
301 advvpasgel vrrytstllp gdtwaqqtfr vehwpnetsv qangsfvrat vhdryrlvnr
361 nlsisenrtm qlavlvndsd fqgpgagvll lhfnsvlvpv slhlpstysl svsrarrffa
421 qigkvcvenc qafsginvqy klhssgancs tlgvvtsaed tsgilfvndt kalrrpkcae
481 lhymvvatdq qtsrqagaql lvtvegsvya eeagcplscs vskrrlecee cgglsptgr
541 cewrqgdgkq itrnfstcsp stktcpdghc dvvetqdini cpqdcrlgsi vgghepgepr
601 gikagygtcn cfpeeeckfc epediqdplc delcrtviaa avlfsfivsv llsafcihcy
661 hkfahkppis saemtfrpa qafpvsvsyss garrpsldsm enqvsvdafk iledpkwefp
721 rknlvlgktl gegefkgkvk atafhlkgra gyttvavkml kenaspseir dllsefnvlk
781 qvnphphvikl ygacsqdgpl lliveyakyg slrgflresr kvpgpylgsg gsrnssldh
841 pderaltmgd lisfawqisq gmqylaemkl vhrdlaarni lvaegrkmki sdfglrsdvy
901 eedsyvkrsq gripvkwmai eslfdhiytt qsdvwsfgvl lweivtlggn pypgipperl
961 fnllktghrm erpdncseem yrmlqcwkk epdkrpvfad iskdlekmmv krrdyldlaa
1021 stpsdsliyd dglseeetpl vdcnnaplpr alpstwienk lygmsdpnwp gespvpltra
1081 dgtntgfpri pndsvyanwm lspsaaklmd tfds
```

//

[Disclaimer](#) | [Write to the Help Desk](#)
[NCBI](#) | [NLM](#) | [NIH](#)

Last update: Mon, 12 Jan 2009 Rev. 149544